

(1) *Definitions.* For the purpose of this section:

(i) *Minor use* means the use of: (a) New animal drugs in minor animal species, or (b) new animal drugs in any animal species for the control of a disease that (1) occurs infrequently or (2) occurs in limited geographic areas.

(ii) *Minor species* means animals other than cattle, horses, swine, chickens, turkeys, dogs, and cats.

(2) *Animal safety, effectiveness, human food safety, and environmental considerations.* Guidance documents for the preparation and submission of data to satisfy the requirements of section 512 of the act regarding animal safety, effectiveness, human food safety, and environmental considerations for new animal drugs intended for a *minor use* (as defined in paragraph (d)(1)(i) of this section) are available from the Industry Information Staff (HFV-11), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855.

(i) *Animal safety and effectiveness.* Where the guidance documents do not specifically provide for a particular *minor use*, the Center for Veterinary Medicine, upon request, will advise interested persons on the effectiveness and animal safety data regarding the minor use that will be needed to satisfy the requirements of section 512 of the act. Where scientifically appropriate, the Center for Veterinary Medicine will allow the use of animal models and the extrapolation of data from a major species to a minor species to satisfy the requirements of the act.

(ii) *Human food safety and environmental considerations.* These guidance documents do not specifically provide for a particular *minor use*. Therefore, the Center for Veterinary Medicine will, upon request, advise interested persons of the data that will be needed. Where scientifically appropriate, the Center for Veterinary Medicine will allow the extrapolation of data from a major species to a minor species to satisfy the requirements of the act.

[40 FR 13825, Mar. 27, 1975]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting §514.1, see the List of CFR Sections Affected, which appears in the Finding Aids section of the printed volume and on GPO Access.

§514.3 Definitions.

The definition and interpretation of terms contained in this section apply to those terms as used throughout subchapter E.

(a) *Adverse drug experience* is any adverse event associated with the use of a new animal drug, whether or not considered to be drug related, and whether or not the new animal drug was used in accordance with the approved labeling (i.e., used according to label directions or used in an extralabel manner, including but not limited to different route of administration, different species, different indications, or other than labeled dosage). Adverse drug experience includes, but is not limited to:

(1) An adverse event occurring in animals in the course of the use of an animal drug product by a veterinarian or by a livestock producer or other animal owner or caretaker.

(2) Failure of a new animal drug to produce its expected pharmacological or clinical effect (lack of effectiveness).

(3) An adverse event occurring in humans from exposure during manufacture, testing, handling, or use of a new animal drug.

(b) *ANADA* is an abbreviated new animal drug application including all amendments and supplements.

(c) *Applicant* is a person who owns a new animal drug application or ANADA.

(d) *Increased frequency of adverse drug experience* is an increased rate of occurrence of a particular serious adverse drug event, expected or unexpected, after appropriate adjustment for drug exposure.

(e) *NADA* is a new animal drug application including all amendments and supplements.

(f) *Nonapplicant* is any person other than the applicant whose name appears on the label and who is engaged in manufacturing, packing, distribution, or labeling of the product.

(g) *Product defect/manufacturing defect* is the deviation of a distributed product from the standards specified in the approved application, or any significant chemical, physical, or other change, or deterioration in the distributed drug product, including any microbial or chemical contamination. A

manufacturing defect is a product defect caused or aggravated by a manufacturing or related process. A manufacturing defect may occur from a single event or from deficiencies inherent to the manufacturing process. These defects are generally associated with product contamination, product deterioration, manufacturing error, defective packaging, damage from disaster, or labeling error. For example, a labeling error may include any incident that causes a distributed product to be mistaken for, or its labeling applied to, another product.

(h) *Serious adverse drug experience* is an adverse event that is fatal or life-threatening, requires professional intervention, or causes an abortion, stillbirth, infertility, congenital anomaly, prolonged or permanent disability, or disfigurement.

(i) *Unexpected adverse drug experience* is an adverse event that is not listed in the current labeling for the new animal drug and includes any event that may be symptomatically and pathophysiologically related to an event listed on the labeling, but differs from the event because of greater severity or specificity. For example, under this definition hepatic necrosis would be unexpected if the labeling referred only to elevated hepatic enzymes or hepatitis.

EFFECTIVE DATE NOTE: At 67 FR 5057, Feb. 4, 2002, § 514.3 was added, effective Aug. 5, 2002.

§ 514.4 Substantial evidence.

(a) *Definition of substantial evidence.* Substantial evidence means evidence consisting of one or more adequate and well-controlled studies, such as a study in a target species, study in laboratory animals, field study, bioequivalence study, or an in vitro study, on the basis of which it could fairly and reasonably be concluded by experts qualified by scientific training and experience to evaluate the effectiveness of the new animal drug involved that the new animal drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof. Substantial evidence shall include such adequate and well-controlled studies that

are, as a matter of sound scientific judgment, necessary to establish that a new animal drug will have its intended effect.

(b) *Characteristics of substantial evidence*—(1) *Qualifications of experts.* Any study that is intended to be part of substantial evidence of the effectiveness of a new animal drug shall be conducted by experts qualified by scientific training and experience.

(2) *Intended uses and conditions of use.* Substantial evidence of effectiveness of a new animal drug shall demonstrate that the new animal drug is effective for each intended use and associated conditions of use for and under which approval is sought.

(i) *Dose range labeling.* Sponsors should, to the extent possible, provide for a dose range because it increases the utility of the new animal drug by providing the user flexibility in the selection of a safe and effective dose. In general, substantial evidence to support dose range labeling for a new animal drug intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease must consist of at least one adequate and well-controlled study on the basis of which qualified experts could fairly and reasonably conclude that the new animal drug will be effective for the intended use at the lowest dose of the dose range suggested in the proposed labeling for that intended use. Substantial evidence to support dose range labeling for a new animal drug intended to affect the structure or function of the body of an animal generally must consist of at least one adequate and well-controlled study on the basis of which qualified experts could fairly and reasonably conclude that the new animal drug will be effective for the intended use at all doses within the range suggested in the proposed labeling for the intended use.

(ii) [Reserved]

(3) *Studies*—(i) *Number.* Substantial evidence of the effectiveness of a new animal drug for each intended use and associated conditions of use shall consist of a sufficient number of current adequate and well-controlled studies of sufficient quality and persuasiveness to permit qualified experts:

(A) To determine that the parameters selected for measurement and the